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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,799	03/24/2004	Randall K. Wetzel	CST-214	4415

7590 04/09/2008

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
04/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/807,799	WETZEL ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *9-14* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 15* is/are rejected.

7)☐ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8, 15 are examined in the instant application.

Withdrawn Rejection

The following rejections have been withdrawn: 1) Objection to the specification, 2) 112, second paragraph, 3) 112, first paragraph, deposit, written description and enablement, In view of the amendment and/or arguments.

Drawing

The response asserts that that the application as filed on March 24, 2004 included 3 sets of color drawings and a statement regarding color drawings was made on page 5 lines 20-24 of the specification. The response asserts that an artifact sheets from PAIR (Tab A) show that the color drawings were submitted.

The response has been considered but is not found to be persuasive for the following reasons:

Although three sets of color drawings are submitted, a petition, and an appropriate fee have not been submitted, as required under 37 CFR 1.84(a)(2) and 37 CFR 1.17(h).

NEW REJECTON BASED ON NEW CONSIDERATION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Denderen et al, 1989, J Exp Med, 169:87-98, IDS of 06/14/05, as evidenced by WO/200269900-A2 (Fritz et al, 09/12/2002), Denderen et al, 1993, Leukemia and Lymphoma, 11: 29-32, IDS of 06/14/05, and US 5,369,008 (Arlinghaus et al, filed on 11/12/1993).

Claims 1-3 are as follows:

1. (Previously Presented) An isolated antibody that specifically binds to human P210 BCR-ABL fusion protein (SEQ ID NO: 1), but does not bind wild type BCR or wild-type c-ABL.

2. (Previously Presented) The antibody of claim 1, wherein said antibody binds a polypeptide comprising residues 94 to 108 of SEQ ID NO: 1.

3. (Previously Presented) The antibody of claim 1, wherein said antibody binds a P210 BCR-ABL polypeptide comprising fusion joint residues 97 to 101 of SEQ ID NO: 1.

Denderon et al, 1989, teach an **antibody** to the tumor specific **bcr-abl joining region**, using as antigen the peptide representing the junction of the b2a2 P210 bcr-abl fusion protein (Summary on page 96, p.89, item under Results, bridging p.90, and p.95, last three paragraphs). Denderon et al, 1989, teach that the antibody recognizes the bcr-abl junction in native p210 bcr-

abl (p.96, summary). Denderon et al, 1989, teach that the antibody only precipitates the P210 bcr-abl fusion protein in the CML cell line BV173 cell, which has a molecular weight of 210 Kd, comprising a portion of bcr protein and a portion of abl protein (p.87, first paragraph, p.92, last paragraph, figure 5 on page 94). Denderon et al, 1989, teach that the antibody does not bind to the a2 part (ABL part) of the junction peptide BCR-ABL (p.93, first paragraph). Denderon et al teach that the antibody **recognizes the joining region itself, or the newly created tertiary b2 or a2 determinants** introduced by the bcr-abl joining region (p.95, last three paragraphs).

The antibody taught by Denderon et al, 1989, would bind to the human P210 BCR-ABL fusion protein, SEQ ID NO:1, or bind to a polypeptide "comprising" residues 94-108 or 97-101 of SEQ ID NO:1, because the human P210 BCR-ABL fusion protein is known in the art, as evidenced by WO/200269900-A2. WO/200269900-A2 teaches a human BRC/ABL fusion sequence, SEQ ID NO:21 (p.20), which is the same as the claimed human BCR/ABL fusion protein SEQ ID NO:1 (MPSRCH search result, 2008, us-10-807-799.1.rag, result 1, pages 1-2).

The antibody taught by Denderon et al, 1989, would not bind to wild type BCR, as evidenced by Denderon et al,1993. Denderon et al, 1993, teach that an antibody to bcr alone precipitates two proteins with lower molecular weight than the p210 in the CML cell line BV173 cell (figure 1-B, lane 2 on page 31). In view that the antibody to the bcr-abl joining region of p210 taught by Denderon et al, 1989, only binds to one protein at 210 kd, the data by Denderon et al, 1993, indicates that the antibody to the bcr-abl joining region of p210 taught by Denderon et al, 1989, is specific for p210, and does not bind to the wild type BRC, represented by the two proteins having lower molecular weights than p210, and detected by the antibody to bcr alone.

Further, the antibody taught by Denderon et al, 1989, would not bind to the wild type ABL, because Denderon et al, 1989, teach that the antibody does not bind to the a2 part (ABL part) of the junction peptide BCR-ABL, and as evidenced by US 5,369,008, which teaches that ABL protein has a molecular weight of 145 Kd (p145 in figure 1, and its legend on column 2, lines 50-53). In view that the antibody to the bcr-abl joining region of p210 taught by Denderon et al, 1989, only binds to one protein at 210 kd, the data by US 5,369,008 indicates that the antibody to the bcr-abl joining region of p210 taught by Denderon et al,1989, is specific for p210, and does not bind to the wild type ABL, represented by the 145 Kd protein.

Although the references do not explicitly teach that the antibody to P210 BCR-ABL binds to the human P210 BCR-ABL SEQ ID NO:1, but does not bind to wild type BCR or wild type c-ABL, however, the claimed antibody appears to be the same as the prior art antibody. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Denderen et al, 1989, J Exp Med, 169:87-98, IDS of 06/14/05, as evidenced by WO/200269900-A2 (Fritz et al, 09/12/2002), Denderen et al, 1993, Leukemia and Lymphoma, 11: 29-32, IDS of 06/14/05, and US 5,369,008 (Arlinghaus et al, filed on 11/12/1993), and in view of US 6,617,119 (Prusiner et al, filed on 07/09/2001).

Claims 1-7, 15 are as follows:

1. (Previously Presented) An isolated antibody that specifically binds to human P210 BCR-ABL fusion protein (SEQ ID NO: 1), but does not bind wild type BCR or wild-type c-ABL.

2. (Previously Presented) The antibody of claim 1, wherein said antibody binds a polypeptide comprising residues 94 to 108 of SEQ ID NO: 1.

3. (Previously Presented) The antibody of claim 1, wherein said antibody binds a P210 BCR-ABL polypeptide comprising fusion joint residues 97 to 101 of SEQ ID NO: 1.

4. (Currently Amended) The antibody of claim 1, wherein said antibody specifically detects P210 BCR-ABL fusion protein in a cell-assay selected from the group consisting of flow cytometry (FC), immunohistochemistry (IHC), or immunofluorescence (IF).

5. (Original) The antibody of claim 1, wherein said antibody is monoclonal.

6. (Original) An immortalized cell line producing the antibody of claim 5.

7. (Original) The cell line of claim 6, wherein said cell line is a hybridoma.

15. (Previously Presented) A kit for the detection of P210 BCR-ABL fusion protein in a biological sample, said kit comprising at least one detectable antibody of claim 1.

The teaching of Denderon, 1989, 1993, WO/200269900-A2 and US 5,369,008 has been set forth above.

Denderon, 1989, 1993, WO/200269900-A2 and US 5,369,008 do not specifically teach that the antibody binds to the human P210 BCR-ABL fusion protein, SEQ ID NO:1, but does not bind to wild type BCR or wild type c-ABL. Denderon, 1989, 1993, WO/200269900-A2 and US 5,369,008 do not teach a cell assay, using immunofluorescence. Denderon, 1989, 1993, WO/200269900-A2 and US 5,369,008 do not teach monoclonal antibody, a cell line or a

hybridoma producing the monoclonal antibody. Denderon, 1989, 1993, WO/200269900-A2 and US 5,369,008 do not teach a kit comprising the antibody.

US 6,617,119 teaches polyclonal and monoclonal antibody specific to **conformation** of a protein associated with diseases, and a hybridoma producing the monoclonal antibody, for detecting diseases (columns 22-23). US 6,617,119 teaches immunoassay using the labeled antibody, for detecting the radioactive or fluorescent signal (columns 7-8, and column 17, first paragraph).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to make an antibody specific for the conformation of the BCR-ABL fusion protein at the junction of BCR-ABL, as suggested by Denderon et al, using the method taught by US 6, 617,119, for detecting cancer, such as CML, as suggested by Denderon et al.

It would have been obvious to make monoclonal antibody to the BCR-ABL fusion protein at the junction of BCR-ABL, and its hybridoma using the method taught by US 6,617,119, because monoclonal antibody would be more selective than polyclonal antibody.

It would have been obvious to formulate the antibody taught by the combined art in a kit for commercial application.

One would have expected that the antibody taught by the combined art would not bind to the wild type BCR or wild type c-ABL, because the antibody taught by the combined art is specific for the conformation of the BCR-ABL junction region, which conformation or tertiary determinant is newly created by the joining of bcr-abl as taught by Denderon et al, and thus would not exist in the wild type BCR or wild type c-ABL.

MPSRCH search result

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US-10-807-799-1.RAG
RESULT 1
ABG95017
ID   ABG95017 standard; protein; 307 AA.
XX
AC   ABG95017;
XX
DT   04-DEC-2002  (first entry)
XX
DE   Human translocation (9: 22)(q34: q11) protein #9.
XX
KW   Chromosome aberration; oncogenic fusion protein; cancer;
KW   proliferative disease; cellular protein isoform; heat shock protein 90;
KW   HSP-90; rheumatoid arthritis; cancer; haematopoietic disorder;
KW   T cell lymphona; B cell lymphoma; chronic myeloid leukaemia; CML;
KW   acute myeloid leukaemia; AML; chronic myelomonocytic leukaemia; CMML;
KW   acute lymphoblastic leukaemia; ALL; APL; NHL; solid tumour;
KW   papillary thyroid carcinoma; Ewing's sarcoma; melanoma; liposarcoma;
KW   rhabdomyosarcoma; synovial sarcoma; viral infection.
XX
OS   Homo sapiens.
XX
PN   WO200269900-A2.
XX
PD   12-SEP-2002.
XX
PF   01-MAR-2002; 2002WO-US006518.
XX
PR   01-MAR-2001; 2001US-0272751P.
XX
PA   (CONF-) CONFORMA THERAPEUTICS CORP.
XX
PI   Fritz LC,  Burrows FJ;
XX
DR   WPI; 2002-698710/75.
DR   N-PSDB; ABS73180.
XX
PT   Treating genetically-defined disease associated with chromosomal
PT   aberrations yielding oncogenic fusion proteins, e.g. cell proliferative
PT   diseases, involves administering an inhibitor of heat shock protein 90.
XX
PS   Claim 28; Page 99-100; 389pp; English.
XX
CC   The invention describes a method of treating genetically-defined disease
CC   associated with chromosomal aberrations yielding oncogenic fusion
CC   proteins (I), treating cancerous cells containing (I) in a heterogeneous
CC   cell population, treating proliferative diseases associated with mutant
CC   protein or cellular protein isoforms (II) dependent on heat shock protein
CC   (HSP)-90, or selectively treating cells expressing (II) involving
CC   administering HSP90-inhibitor. The method is useful for treating
CC   genetically-defined disease with chromosomal aberration yielding
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CC   oncogenic fusion protein, treating cancerous cells containing fusion
CC   protein in heterogeneous cell population, treating proliferative disease
CC   (e.g. rheumatoid arthritis or cancer) associated with mutant protein or
CC   cellular protein isoform dependent on heat shock protein (HSP)-90 (e.g.
CC   p53), or selectively treating cells expressing mutant protein or cellular
CC   protein isoform in a patient heterozygous for (II). The method is useful
CC   for treating a disease e.g. haematopoietic disorder such as T or B cell
CC   lymphoma, chronic myeloid leukaemia (CML), APL, ALL, AML, NHL and CMML,
CC   or a disease characterised by a solid tumour such as papillary thyroid
CC   carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma and
CC   synovial sarcoma. The method is also useful for treating viral
CC   infections. This represents a protein encoded by the DNA sequence of a
CC   chromosome aberration
XX
SQ   Sequence 307 AA;

  Query Match             100.0%;  Score 1604;  DB 5;  Length 307;
  Best Local Similarity   100.0%;  Pred. No. 2.5e-146;
  Matches  307;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 ANKGSKATERLKKKLSEQESLLLLMSPSMAFRVHSRNGKSYTFLISSDYERAEWRENIRE 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ANKGSKATERLKKKLSEQESLLLLMSPSMAFRVHSRNGKSYTFLISSDYERAEWRENIRE 60

Qy         61 QQKKCFRSFSLTSVELQMLTNSCVKLQTVHSIPLTINKEEALQRPVASDFEPQGLSEAAR 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 QQKKCFRSFSLTSVELQMLTNSCVKLQTVHSIPLTINKEEALQRPVASDFEPQGLSEAAR 120

Qy        121 WNSKENLLAGPSENDPNLFVALYDFVASGDNTLSITKGEKLRVLGYNHNGEWCEAQTKNG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 WNSKENLLAGPSENDPNLFVALYDFVASGDNTLSITKGEKLRVLGYNHNGEWCEAQTKNG 180
Qy        181 QGWVPSNYITPVNSLEKHSWYHGPVSRNAAEYLLSSGINGSFLVRESESSPGQRSISLRY 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 QGWVPSNYITPVNSLEKHSWYHGPVSRNAAEYLLSSGINGSFLVRESESSPGQRSISLRY 240

Qy        241 EGRVYHYRINTASDGKLYVSSESRFNTLAELVHHHSTVADGLITTLHYPAPKRNKPTVYG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 EGRVYHYRINTASDGKLYVSSESRFNTLAELVHHHSTVADGLITTLHYPAPKRNKPTVYG 300

Qy        301 VSPNYDK 307
              |||||||
Db        301 VSPNYDK 307
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Conclusion

Claim 8 appears to be free of prior art but is objected to as being dependent upon rejected base claims, but would be allowable if rewritten in independent forms.

Claims 1-7, 15 are rejected for the reasons set forth above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
April 06, 2008

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643